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MEMORANDUM

TO: Denise Webster
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HSM-02038

FROM: Wendy Zhao
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VIA: Joseph P. Frank
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Work Health and Safety Branch

DATE: October 4, 2002

SUBJECT: PRODUCT NAME: Chlorpyrifos
ACTIVE INGREDIENT: Chlorpyrifos
I.D. NUMBER: SBRA 185237E
DOCUMENT PACKAGE NUMBER (DPN): 342-813
EPA REGISTRATION NUMBER: --
TITLE: Response to Comments from Dow AgroSciences LLC on the Draft
Chlorpyrifos Risk Characterization Document by the California
Department of Pesticide Regulation (Exposure Assessment Section)

In September of 2000, Dow AgroSciences (DAS) LLC submitted comments on the draft chlorpyrifos risk characterization document prepared by the California Department of Pesticide Regulation (DPR). Most comments were focused on risk assessment and have been responded by the Medical Toxicology (Med Tox) Branch. This memorandum addresses the comments on the exposure assessment section.

The comments from DAS are presented in italic characters, and the DPR responses are presented in non-italic characters.

1. Dermal Absorption Rate

DAS: Dermal absorption of low doses in a new published study was about 1% (Griffin et al., 1999), comparable to that reported by Nolan et al., (1984) and appreciably lower than the 9.6% reported by Thongsinthusak et al. (1993).

DPR: Thongsinthusak (1999) had evaluated the new dermal absorption study conducted by Griffin et al. (1999). The Worker Health and Safety (WHS) Branch considered this study unacceptable due to the following two main reasons:

- 1) Dermal dose was too high compared to typical chlorpyrifos dermal exposure levels.



The U.S. EPA dermal absorption study guidelines recommend that doses should span the range of doses expected in field exposures (Zendzian, 1994). The exposure assessment for chlorpyrifos indicated that mean dermal exposure estimates for chlorpyrifos ranged from 0.2 to 4 $\mu\text{g}/\text{cm}^2$ for field workers and 0.2 to 0.7 $\mu\text{g}/\text{cm}^2$ for children playing in treated homes. In the study conducted by Griffin et al. (1999), about 29 mg of chlorpyrifos was administered to an area of 78 cm^2 of the inner forearm of volunteers, i.e., about 371 $\mu\text{g}/\text{cm}^2$. This dose is much higher than the range of dermal exposures as mentioned above. It was indicated that the percentage of dermal absorption for most pesticides is higher when the dose is lower (Wester and Maibach, 1993; Thongsinthusak et al., 1999).

2) Poor mass balance.

In the dermal absorption study conducted by Griffin et al. (1999), 1% of the administered dose was excreted as dialkylphosphate metabolites and 53% was recovered as chlorpyrifos from skin washings. That means up to 46% of the administered dose was not recovered. The possibility that some of the unaccounted dose might be absorbed cannot be excluded.

Based on the above rationales, WHS considered that the dermal absorption study performed by Griffin et al. (1999) was unacceptable. WHS decided to continue using the extrapolated dermal absorption rate of 9.6% (Thongsinthusak, 1991) as the best available estimate of dermal absorption for chlorpyrifos.

2. Residential Exposure Assessments

DAS: In order to bring closure to the original concerns for the re-evaluation of chlorpyrifos, CA EPA has conducted exposure assessments on use patterns that are no longer labeled or allowed such as indoor broadcast treatments...Although this rationale to include the exposure assessments makes sense given the qualifier noted, it would better clarify to the reader if the document officially acknowledged that these use patterns are no longer labeled for use and as such exposures have therefore been successfully mitigated...

DPR: In June, 2000, the United States Environmental Protection Agency (U.S. EPA) entered into an agreement with the technical registrants to eliminate virtually all homeowner uses (except ant and roach baits in child resistant packaging) to reduce certain residential risks. The exposure assessments for these uses were retained in the exposure assessment document because of initial exposure concerns that triggered the reevaluation process for chlorpyrifos. This rationale had been mentioned in the exposure assessment (see page 2). However, WHS would add the following statement in "Exposure Appraisal" section:

E. 3 Cancellation of residential uses.

In June, 2000, the United States Environmental Protection Agency (U.S. EPA) entered into an agreement with the technical chlorpyrifos registrants to eliminate virtually all homeowner uses (except ant and roach baits in child resistant packaging) to reduce certain residential risks. However, the exposure assessments for these uses were retained because of initial exposure concerns that triggered the reevaluation process for chlorpyrifos. Additionally, considering the residents who may use existing stocks of chlorpyrifos, their potential exposure was assessed in the exposure assessment document. If the remaining stocks in homes are exhausted, then such residential exposures have been successfully mitigated.

Use Pattern

DAS: ...To help provide a better understanding of actual chlorpyrifos urban pest market usage, DAS commissioned a small qualitative market research study from MarQuest and a lawn care chlorpyrifos applicator use study from Jefferson Davis during 1999.

...The information from these two surveys can be used to further advance risk assessments for these uses. ...

DPR: WHS determined that the information from MarQuest and Jefferson Davis listed on page 37 – 38 of DAS' document for comments was not enough to assess exposure assessment, e.g., there were no exposure data, no personal protective equipment (PPE) description... The important point is without a completed study document, WHS could not evaluate these isolated numbers for use in exposure assessment.

Without chlorpyrifos-specific data, WHS determined the use rate per acre (or per 100 gallons), PPE requirement, application equipment, crops, etc., basing on product labels, and determined use patterns basing on pesticide use report (PUR) and insecticide generic use databases.

Page 3 (This and subsequent page numbers are referred to page numbers in the chlorpyrifos exposure document, HS-1661, dated September 10, 1999)

DAS: DAS feels that the use of the word "poisoning" should be replaced with the more applicable word "exposure" and that the word "toxic" should be deleted since hazard is related to dose and exposure which has not been addressed in this sentence.

DPR: WHS agrees with the DAS' suggested modifications. The suggested modifications will be used in future revision of the exposure document.

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DAS: Although many products containing chlorpyrifos are currently registered for indoor and outdoor use by homeowners, the task force of technical chlorpyrifos registrants submitted a proposal in 1996 to the U.S. EPA for withdrawal of selected chlorpyrifos products from the indoor home use market.

DAS suggested that “selected” be added as shown in the above sentence.

DPR: WHS agrees with the DAS’ suggested modification. The exposure document will incorporate the suggestion into future revision.

Page 18 (Indoor crack and crevice application)

DAS: The exposure would be expected to be less because the termite applications require the handling of a more concentrated mixture (1% a.i. compared to 0.5% a.i.), and the use of greater volumes of spray mix (typically 100 – 150 gallons of dilute spray mixture compared to less than one gallon of spray mixture per structure).

DAS suggested substituting “(typically 100 – 150 gallons of dilute spray mixture compared to less than one gallon of spray mixture per structure)” for “(one gallon of mix per 10 ft² compared to one gallon of spray mixture per 1600 ft²)”.

DPR: WHS agrees with the DAS’ suggested modification. The exposure document will incorporate the suggestion into future revision.

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DAS: Current research by MarQuest and Jefferson Davis indicates the median use scenarios to be the following as a revision to that used in table III...

DPR: As mentioned above, without a completed study, WHS could not evaluate and use the data from MarQuest and Jefferson Davis for exposure assessment.

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DAS: The maximum rate for home garden products is 2 lb a.i./acre for control of grubs so the rate referred to is actual label language and not an overage.

DAS provided the above suggestion regarding the application rate for control of grub.

DPR: WHS agrees with DAS on the rate of use. The exposure document will incorporate this information into future revision.

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DAS: Of particular concern are the illnesses reported by office workers and homeowners who become ill after entering a treated area. A priori, it is not possible to determine whether the illnesses are caused by (a) the active ingredient, (b) formulation constituents, (c) manufacturing impurities, or (d) other unrelated causes

DAS suggested a statement, “or (d) other unrelated causes”, to explanation of the illnesses reported by office workers and homeowners who became ill after entering a treated area.

DPR: WHS agrees with DAS. The suggested statement will be incorporated into the exposure document in future revision.

3. Ag Occupational Exposure Assessments

No response necessary.

References:

- Griffin, P., Mason, H., Heywood, K., and Cocker, J. 1999. Oral and dermal absorption of chlorpyrifos: a human volunteer study. *Occup. Environ. Med.* 56:10-13.
- Nolan, R. J., Rick, D. L., Freshour, N. L., and Saunders, J. H. 1984. Chlorpyrifos: Pharmacokinetics in human volunteers following oral and dermal doses. *Toxicol. Appl. Pharmacol.* 73:8-15.
- Thongsinthusak, T. 1991. Determination of dermal absorption of chlorpyrifos in humans. HSM-91002. Sacramento, CA: Worker Health and Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency.
- Thongsinthusak, T. 1999. Oral and dermal absorption of chlorpyrifos: A human volunteer study (Griffin et al.). A memorandum dated January 29, 1999, to Karen Fletcher of DPR. Sacramento, CA: Worker Health and Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency.
- Thongsinthusak, T., Ross, J.H. and Dong, M.H. 1999. Significance of dermal dose levels in dermal absorption studies of pesticide. HS-1801. Sacramento, CA: Worker Health and

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Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency. The poster was presented at the Society for Risk Analysis Annual Meeting, December 5-8, 1999, Atlanta, Georgia.

- Wester, R. C., and Maibach, H. I. 1993. Animal models for percutaneous absorption. In *Health Risk Assessment: Dermal and Inhalation Exposure and Absorption of Toxicants*, eds. Wang, R. G. M., Knaak, J. B., and Maibach, H. I. CRC Press, London. pp. 89-103.
- Zendzian, R. P. 1994. Dermal Absorption of Pesticides. Pesticide Assessment Guidelines. Subdivision F, Hazard Evaluation: Human and Domestic Animals. Series 85-3. Health Effect Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C.

Attachment

cc: Ms. Ann Prichard, Pesticide Registration Branch (w/o attachment)